Microfluidic Device for Compartmentalized Coculture of Neuronal and Muscle Cells to Model Motor Neuron Disease

Technology #18042-20857

Applications

This technology is a microfluidic device for the three-dimensional coculture of human neurons and muscle cells to form the neuromuscular junction and a complete motor unit *in vitro*, which can be used to model motor neuron disease pathophysiology and identify novel therapeutics.

Problem Addressed

Amyotrophic lateral sclerosis (ALS) is caused by loss of motor neurons and muscle atrophy, which leads to progressive neurodegeneration. It is estimated that 12,000-15,000 people in the US are living with ALS. While the identification of therapies for ALS is an area of active research, existing treatments for ALS are ineffective. Drug screening for ALS has been traditionally low-throughput due to use of genetically engineered mouse models. Additionally, *in vitro* drug screening attempts have been conducted on incomplete models of the neuromuscular junction. This invention is a microfluidic device that models the human neuromuscular motor unit in 3D space, facilitating *in vitro* human disease modeling and higher-throughput drug screening for ALS and other motor neuron diseases.

Technology

This microfluidic device produces a 3D model of the human neuromuscular junction using coculture chambers divided into three compartments. The first compartment receives myoblasts in collagen hydrogel, which form muscle bundles that wrap around pillars in the chamber. A second compartment receives individual neurospheres suspended in collagen hydrogel. Neurospheres are positioned with respect to muscle bundles to optimize neuromuscular junction formation. The third compartment resides between the muscle and neuronal compartments and serves as a buffer region for neuronal axons to navigate towards muscle cells, thus forming neuromuscular junctions.

This system can be comprised of normal muscle and neuronal components to study the biology of the normal neuromuscular junction, or it can contain motor neuron disease patient-derived neuronal components to model diseases such as ALS. Contraction of 3D muscle fibers can be induced using light and is measured by pillar deflection in the muscle compartment. The degree of pillar deflection is measurable and facilitates detection of neuromuscular defects and potential restoration of neuromuscular function by drug treatment. Multiple cultures can be prepared in parallel with high reproducibility for treatment with candidate drugs in a high-throughput manner.

Advantages

- Compartmentalized 3D coculture design provides functional readout of neuromuscular health
- Device forms microphysiological 3D models of ALS and has potential to model other motor neuron diseases
- *In vitro* design facilitates high-throughput drug screening for motor neuron diseases

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Intellectual Property

IP Type: Granted US Patent

IP Title: Microfluidic device for three dimensional and compartmentalized coculture of neuronal and muscle cells, with functional force readout

IP Number: 10,767,149

IP Type: Published PCT Application

IP Title: Microfluidic device for three dimensional and compartmentalized coculture of neuronal and muscle cells, with functional force readout

IP Number: WO 2017-218581

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IP Title: A micro physiological model for neuronal and muscular diseases and disorders

IP Number: WO 20202-09843

Categories For This Invention:

Life Sciences
Clinical Applications
Neurology
Diagnostics
Microfluidics (Diagnostics)
Research Tools
Microfluidics (Research Tools)
Screening Assays

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Publications:

Microfluidic Device for the Formation of Optically Excitable, Three-Dimensional, Compartmentalized Motor Units
Science Advances
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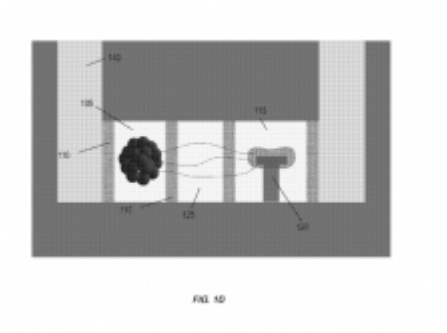
Microphysiological 3D Model of Amyotrophic Lateral Sclerosis (ALS) from Human iPS-Derived Muscle Cells and Optogenetic Motor Neu
Science Advances
October 10, 2018, 4(10), eaat5847.

External Links:

Roger Kamm Research Group
http://web.mit.edu/meche/mb/kamm-mb/people.html

Image Gallery:



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